

Remarks

Claims 1-18 are pending in the subject application. By this Amendment, Applicant has amended claims 1, 4, 5, 7, and 11, and has added new claims 19-21. Support for the new claims and amendments can be found throughout the subject specification, including, for example, at page 3, lines 9-10, and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-21 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Claims 1-18 are objected to under 37 CFR §1.75 as a substantial duplicate of claims 1, 3-17, 21, and 30-37 of parent Application No. 09/463,549, now U.S. Patent No. 7,008,766 (hereinafter the '766 patent). Applicant respectfully asserts that the claims in the subject application are not substantial duplicates of claims in the '766 patent. The scope of independent claim 1 of the present application and claim 1 of the '766 patent is different. Accordingly, reconsideration and withdrawal of the objection under 37 CFR §1.75 is respectfully requested.

Claims 1-18 are provisionally rejected for "obviousness-type" double patenting over claims 1, 3-17, 21, and 30-37 of parent Application No. 09/463,549, now U.S. Patent No. 7,008,766. Applicant respectfully asserts that the claims of the subject application are not obvious over the claims of the '766 patent. However, in order to expedite prosecution of the subject application to completion, attached with this Amendment is a Terminal Disclaimer which obviates the rejection. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-18 are rejected under 35 USC §112, first paragraph, as nonenabled and as lacking adequate written description in the subject specification. Specifically, the Examiner indicates that the subject specification does not contain a reproducible method whereby any nucleic acid could be sequenced to completion, wherein the length of the nucleic acid can be unlimited, and wherein the nucleic acid can be "present in a heterogeneous mixture of other polynucleotides, and/or where all possible nucleotides are present and nascent sequences are allowed to develop unimpeded." The Examiner also asserts, at least in regard to claim 7, that the subject specification speculates as to the ability to practice certain elements of the invention and, therefore, does not teach that the inventors were in possession of the claimed invention as of the filing date of the application. The Examiner also asserts that the specification does not enable the claimed method whereby dual blocking groups are utilized and can be selectively removed.

Applicant respectfully asserts that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention and that the claims are enabled by the subject specification. Applicant notes that claim 1 has been amended to clarify that, in practicing the claimed method, each complementary nucleotide that is incorporated during the processing of the polymerase is detected. This provides that the nucleotide sequence of the polynucleotide can be determined regardless of the speed of the reaction. Applicant also notes that claims 2-18, as amended, read substantially the same as the dependent claims in the '766 patent, which were determined to have adequate written description and enablement by the Patent Office.

In regard to the issue of polynucleotide length, Applicant respectfully asserts that the claimed method can be used with any length polynucleotide. There is no evidence to suggest an upper limit on length of the polynucleotide that can be sequenced using the claimed method. The Examiner also indicates that the issue of length of the polynucleotide also raises the possibility of self-self duplex formation. Applicant respectfully notes that polymerases can "undo" self-self duplexes and continue processing along the polynucleotide strand.

In regard to the issue of sequencing a target polynucleotide in a heterogeneous mixture of polynucleotides, Applicant respectfully notes that the claimed method can utilize any suitable technique to measure a change in or absorption of radiation that occurs during the interaction of the polymerase, the target polynucleotide, and the complementary nucleotide that is incorporated into the nascent polynucleotide during the sequencing reaction. Applicant respectfully submits that techniques, such as surface plasmon resonance (SPR), can be conducted at a very localized region on the solid support and, therefore, can be used in measurements at the single molecule level. Support for this can be found in the subject specification at, for example, page 5, lines 21-33, and page 6, lines 7-14.

Also under these rejections, the Examiner asserts that the claims can be interpreted as encompassing binding of the polymerase to a target polynucleotide where the polynucleotide is bound directly or indirectly to the support. By this Amendment, Applicant has amended claim 1 to specify that the polymerase is itself immobilized on the solid support. Applicant notes, however, that the immobilization of the polymerase to the solid support can be either through direct binding to the support, or through indirect binding, such as by a linker molecule attached to the support wherein

the polymerase is bound to the linker molecule. The Examiner also questions whether sequencing using the claimed method can occur where all possible nucleotides are present in the reaction mixture but wherein the nucleotides do not contain blocking groups. Applicant respectfully asserts that all nucleotides can be present and unblocked in the claimed method. In this situation, the polymerase reaction will occur at a faster rate and, therefore, detection can be achieved using appropriate readout technology.

In regard to claim 7, the Examiner indicates that the subject specification does not provide support for the method where nucleotides that are blocked at both the 3' and 5' end are utilized since it is not clear that the blocking groups can be selectively removed. Applicant respectfully asserts that the subject specification does teach that blocking groups can be used that can be selectively removed based on their spectral absorbance. See, for example, the middle of page 8 through to the middle of page 9 of the subject specification and at page 12 of the subject specification which teach 3' and 5' blocking groups and selective removal thereof.

Applicant respectfully asserts that the claims do find written description and are enabled by the subject specification. In view of the above, reconsideration and withdrawal of the rejections under 35 USC §112, first paragraph, is respectfully requested.

Claims 1-18 are rejected for “obviousness type” double patenting over claims 1-5 of U.S. Patent No. 6,623,929 (hereinafter the ‘929 patent). Applicant respectfully asserts that claims 1-18 in the subject application are not obvious over claims in the ‘929 patent. The ‘929 patent claims are directed to methods for synthesis of a polynucleotide molecule by controlling the conformation of a polymerase enzyme. The claims of the subject invention are directed to methods of obtaining the sequence of a polynucleotide molecule. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-18 are also provisionally rejected for “obviousness-type” double patenting over claims 1, 9, 11-12, 16-17, and 21-22 of co-pending Application No. 10/478,036 (hereinafter the ‘036 application). Applicant respectfully submits that claims 1-18 in the subject application are not obvious over claims in the ‘036 patent application. The claims in the ‘036 application are directed toward detecting the conformation of a polymerase enzyme by measurement of non-linear signals. The claims of the subject application do not involve detection of non-linear signals. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicant's agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicant invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachment: Amendment Transmittal Letter; Terminal Disclaimer